REMARKS

CLAIM AMENDMENTS

The claims have been returned to their original claim language. The reason for the changes to the claims is explained in the discussions that follow below. Claim 1 has been changed slightly from its original format to recite that the vasoactive agent is topically administered. New claim 41 recites that the topical administration of the vasoactive agent is via transmucosal administration. Support for the change to claim 1 is found throughout the specification and in particular at page 23, lines 24-25; page 33, lines 12-14; and the Examples. Support for the change to claim 1 is found throughout the specification and in particular at page 12, lines 10-12 and 21-25; and page 33, lines 27-28. New claims 42, 43, and 44 represent the subject matter of previously canceled claims 3, 4, and 15, respectively. Claim 20 has been amended to depend from new claim 43, rather than canceled claim 4. No new matter has been added to the application with the claim amendments.

THE GROUNDS OF THE OFFICE ACTION OF JULY 23, 2004:

In the Office Action dated March 29, 2004, the Examiner set forth the following prior art rejections:

1. claims 1-2, 6, 11-12, and 14 under 35 U.S.C. § 102(e) over Wysor et al.;
2. claims 1-2, 6-15, and 23-28 under 35 U.S.C. § 103(a) over Ottensen et al., PEPTIDES 8(5):797-800 (1987); and
3. claims 1-15 and 23-29 under 35 U.S.C. § 103(a) over Wysor et al. in view of Ottensen et al., REGULATORY PEPTIDES 11:83-92 (1985).

In the response to the Office Action filed on July 23, 2004 applicants amended the claims such that the rejections were rendered moot. The rejections were traversed, but in light of the claim amendments, no arguments distinguishing the references were deemed necessary. On November 15, 2004, the Notice of Allowance for this matter was mailed from the Office.

THE PRIORITY DATE OF THE INSTANT APPLICATION DISQUALIFIES THE WYSOR ET AL. REFERENCE AS PRIOR ART TO THE CLAIMED INVENTION

Upon review of the priority documents of this application, applicants have found that the Wysor et al. patent is not prior art to the instant application. Specifically, referring the Examiner's attention to the originally filed parent applications, U.S. Patent Application No. 09/959,057, filed on October 28, 1997, now abandoned, and U.S. Patent Application No. 09/959,064, also filed on October 28, 1997, now U.S. Patent No. 5,877,216 ("the '216 Patent"), applicants note that these

two priority documents disclose (and the two documents also originally claimed) VIP agonists and analogs. Referring to the issued '216 Patent, VIP and VIP agonists are referenced in the Abstract, col.1, ll. 24-32; col. 4, ll. 38-39; col. 6, l.58; and col. 7, ll. 34-37.

In light of the foregoing disclosures in the parent applications, both of which have a filing date of October 28, 1997, the disclosure of the instant application predates the January 29, 1999, filing date of the Wysor et al. patent; consequently, the Wysor et al. patent is disqualified as prior art against the claims of the instant application.

THE OTTENSEN ET AL. PEPTIDES REFERENCE DOES NOT TEACH OR SUGGEST TRANSMUCOSAL ADMINISTRATION OF VIP OR VIP AGONISTS

A *prima facie* case of obviousness under 35 U.S.C. § 103 requires a showing that the cited prior art reference teaches or suggests the claimed combination and that the ordinary artisan would have a reasonable expectation of success at arriving at the claimed combination based *solely* on the teachings of the cited prior art reference. *In re Vaeck,* 947 F.2d 488 (Fed. Cir. 1991).

As recited in claim 1, the present invention relates to a method for treating sexual dysfunction in a female individual, comprising topically administering to the vagina and/or vulvar region of the individual a pharmaceutical formulation that comprises a therapeutically effective amount of a vasoactive agent selected from the group consisting of vasoactive intestinal polypeptides, vasoactive intestinal polypeptide agonists, and combinations thereof.

As noted by the Examiner in the first paragraph of page 6 of the Office Action, Ottensen et al. (Peptides) ("Ottensen 1") teaches administration of VIP via intravenous or subepithelial injection. In the Office Action, the Examiner takes the position that the "result-effective adjustment of particular conventional working conditions," i.e., choosing other commonly employed modes of administration, are "merely a matter of judicious selection and routine optimization...well within the purview of the skilled artisan" (Office Action, page 6). The foregoing discussion will show why the Examiner's application of Ottensen 1 against the claimed invention does ***not*** render the claimed invention obvious.

Turning first to the title of Ottensen 1, applicants note that the title of this paper is: "Vasoactive Intestinal Polypeptide (VIP) Provokes Vaginal Lubrication in *Normal Women*" (emphasis added here). The title of Ottensen 1 thus shows that this paper is directed to normal women and not women that are experiencing a condition such as sexual dysfunction; accordingly, this paper is more of an academic exercise directed to determine the physiological role of VIP in

normal sexual behavior, rather than an investigation into the role of VIP in the treatment of women that do not experience normal sexual behavior.

Turning next to the content of the paper, applicants' direct the Examiner's attention to page 797 where the experimental procedure of the paper is described. There, it is provided that fourteen non-pregnant women participated in the study, which included the intravenous administration of saline and VIP at 900 pmol x kg b. wt.$^{-1}$ x h^{-1} using a perfusion pump through the cubital veins on both arms of the patients. Following the administration of the saline and VIP, vaginal transudate in the women was measured (page 798, col. 1) as was peripheral blood from the patients, both being measured every 30 minutes. As explained at column 2 of page 798, the infusion of VIP induced a significant increase in vaginal blood flow and vaginal lubrication in comparison to the preceding and following control periods (Figs. 1-3); however, as noted at the top of column 1 of page 799, none of the patients reported sexual arousal during the experiment. At the bottom of column 1 at page 799, the authors of the paper conclude that the study supports a neurotransmitter role for VIP in the control of physiological responses during sexual arousal. In light of their conclusion, the authors speculate that "neuropathy of VIP containing nerve fibers, i.e., in diabetic patients may lead to impaired regulation of vaginal blood flow as well as lubrication and thereby sexual dysfunction."

The foregoing analysis of Ottensen 1 shows that contrary to the Examiner's assertion, the paper does not lead the ordinary artisan to the topical administration of VIP for the treatment of sexual dysfunction. Not only does Ottensen 1 not teach, suggest, or contemplate the topical administration of VIP, Ottensen 1 also does not contemplate that VIP may have an effect on the treatment of women with sexual dysfunction. As indicated above, based upon the finding of their studies, the authors of Ottensen 1 draw the conclusion that neuropathy of VIP containing nerve fibers may be the cause of sexual dysfunction in diabetic patients. This teaching does not lead the ordinary artisan to the application of VIP to treat diabetic patients experiencing sexual dysfunction; rather, it would lead the ordinary artisan to find a way to prevent or reverse the neuropathy of VIP-containing fibers. Indeed, there is no indication in Ottensen 1 that administration of VIP will lead to a correction of damaged VIP-containing nerve fibers.

Because Ottensen 1 only suggest that sexual dysfunction may be the result of neuropathy of VIP-containing fibers and does not suggest that administration of VIP or VIP agonists may be a solution for the treatment of the sexual dysfunction, it follows that Ottensen 1 does ***not*** teach or suggest the claimed invention. Since Ottensen 1 does not teach or suggest the use of topical VIP or

VIP agonists for the treatment of female sexual dysfunction, it follows that Ottensen 1 does not render the claimed invention obvious.

THE OTTENSEN ET AL. REGULATORY PEPTIDES REFERENCE DOES NOT TEACH OR SUGGEST TRANSMUCOSAL ADMINISTRATION OF VIP OR VIP AGONISTS

The Examiner originally cited Ottensen et al. (referred to herein as "Ottensen 2") as a secondary reference to the teachings of Wysor et al. As explained above, Wysor et al. is disqualified as prior art to the instant application because the priority date of the instant application predates Wysor et al. The Examiner originally cited Ottensen 2 for the teaching of the use of steroids to affect the activity of VIP. With the elimination of Wysor et al., Ottensen 2 holds no weight against the claimed invention.

Ottensen 2 teaches the existence and association between sex steroids and VIP concentration in the genital tract of pregnant rabbits. At the top of page 84, Ottensen 2 explains that the aim of the study disclosed in the paper was to investigate the influence of pregnancy, oophorectomy, estrogen, and/or progesterone treatment on oophorectimized animals, on the tissue concentration of VIP, and on the receptor binding of VIP to muscle membranes. The experiments provided at pages 84-85 show the application of different steroids to pregnant and oophorectomized rabbits, the subsequent termination of the oophorectomized animals after 10 days, and the termination of pregnant rabbits after post-gestation days 9, 19, and 29. Following the termination of the animals, uterine body, cervix, and vagina samples were extracted from the deceased rabbits and the tissue specimens were tested for percentage of VIP via radioimmunoassay using antiserum. As provided at the bottom of page 83 of Ottensen 2, the authors conclude that while sex steroids are able to influence the motor effects of VIP at the receptor level, they have no effect on VIP concentration in the female genital tract.

The foregoing synopsis of Ottensen 2 clearly shows that the purpose of Ottensen 2 is very specific and is directed solely to analyzing the effects of sex steroids on endogenous VIP in the genital tract of the pregnant and oophorectimized rabbits. Nowhere in Ottensen 2 is the administration of VIP discussed, mentioned, or contemplated and nowhere in Ottensen 2 is the effects of VIP on sexual dysfunction addressed. In light of the foregoing, it follows that Ottensen 2 does not teach or suggest the claimed invention; consequently, the teachings of Ottensen 2 do not render the claimed invention obvious.

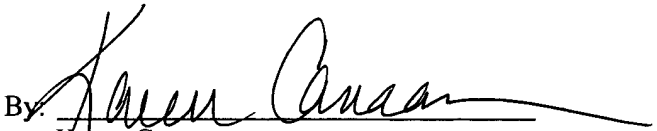
CONCLUSION

This paper, along with the accompanying RCE, was filed so that the Examiner could reopen prosecution to eliminate the Wysor et al. reference from citation against the claimed invention.

As explained above, because the priority date of the instant application predates Wysor et al., this reference is eliminated as prior art against the claimed invention. Since the two remaining references, i.e., Ottensen 1 and Ottensen 2, do not teach or suggest the claimed invention, it follows that a *prima facie* case of obviousness has not been established over the claimed invention. Since the claimed invention is not anticipated or rendered obvious by any of the references cited in the Office Action of July 23, 2004, applicants respectfully request allowance of this application.

Any questions regarding this filing should be directed to the undersigned attorney at 650-330-4913 or canaan@reedpatent.com.

Respectfully submitted,

By: 
Karen Canaan
Registration No. 42,382

REED IP LAW GROUP
800 Menlo Avenue, Suite 210
Menlo Park, California 94025
(650) 330-0900 Telephone
(650) 330-0980 Facsimile